CURRENT SCIENCE

Volume 110 Number 11 10 June 2016

GUEST EDITORIAL

Ayurvedic biology

It is a commentary of our times that European and British adventurers who sought India for conquest and plunder loom large in history books which pay scant attention to the smaller stream of European scholars, scientists, archeologists and engineers who came to India and made a profound impact on life and culture in this country. A striking example is Vasco da Gama of Portugal, who was the first European to reach India by the sea route and is widely celebrated, while another distinguished Portuguese physician – Garcia da Orta – who settled down to practice medicine in Goa for 36 years in the 16th century and pioneered studies in indigenous medicine is hardly known. He wrote *Colloquies on the Simples and Drugs of India* in 1563 based on years of observation on diseases in India, medicinal plants, their use in medicine and his views on the practice of medicine. The book became popular and was translated into several European languages because there was a rush among European nations to explore India, which was believed to be fabulously rich. The would-be explorers were keen to know more about the unfamiliar diseases in the tropics, which had decimated large numbers of Europeans in India. In the 17th century, Van Rheed, the Dutch Governor of Kochi, organized a large group of medicinal botanists, herbal experts, soldier–artists, an Ayurvedic physician, laymen and field workers who studied plants in common use from Kanyakumari to Goa for 30 years and published a classic in 12 volumes – *Hortus Malbaricus* – in Latin. It listed over 700 plants with exquisite illustrations and information on their medical applications. The interest in taxonomy of plants grew rapidly in Europe and India and Linneus systematization became a landmark. After the establishment of the Botanical Survey of India and major studies by Roxburgh in Bengal, Ainslie in Tamil Nadu and several others, taxonomy was at the 'cutting edge' of science in India in the 18th and 19th centuries. It was the favourite tool of biologists to study the role of medicinal plants used in Ayurveda for many centuries.

A new wind blew in the 20th century when Ramnath Chopra joined the new School of Tropical Medicine in Calcutta and began pharmacological studies for the first time in India. His painstaking work involved the botanical identification of plants, isolation of compounds, and extensive studies on their effects *in vivo* and *in vitro* and tests for their toxicity. He aspired 'to make Indian pharmacology self-supporting by enabling her to utilize locally produced drugs economically under standard laboratory conditions and to discover remedies from the claims of Ayurveda, Tibbi and other indigenous sources, suitable to be employed by the exponents of western medicine'. Chopra was acclaimed as the 'Father of Indian Pharmacology', which became the new tool to investigative Ayurveda. This preceded the explosive growth of studies in natural products chemistry in university departments, scientific institutes and industrial laboratories. The wide range and high quality of studies in medicinal plants of Ayurveda by many pioneers such as Asima Chatterjee and T. Govindachari made India a global leader in natural products chemistry. This work continues in the country, though the discovery of a 'block buster' drug has eluded us. The serial inquiries of science over five centuries into Ayurveda through the pathways of taxonomy, pharmacology and natural products chemistry resemble a palimpsest, where the work done earlier is not wiped off before a new text is written. Taxonomy, pharmacology, and natural products chemistry continue to exist with changed objectives and tools in exploring the Ayurvedic quarry. Research in biological sciences was transformed in the 20th century by the discovery of the double helical structure of DNA, which cast a spell on virtually every branch of science and even technology. It was inevitable that Ayurveda, which serves millions of people, would be viewed through the instruments of modern biology in the 21st century. This was anticipated in the decadal vision document 'Towards Ayurvedic Biology' published by the Indian Academy of Sciences in 2006. Thanks to the timely support from the Office of the Principal Scientific Adviser to the Government of India, and the Department of Science and Technology, several collaborative projects between scientific and Ayurvedic institutions were implemented within a decade of the publication of the Vision Document. Projects in Ayurvedic biology are invariably based on the application of scientific methods in the study of Ayurvedic concepts, procedures and mechanistic basis of therapeutic effects. A few examples are given to illustrate the studies.

A basic concept in Ayurveda is prakriti or the constitutional type of individuals, which is fixed at conception

and determines one's predisposition to diseases as well as response to treatment. In every patient, the physician must determine the prakriti on the basis of a number of traits – physical, mental and behavioural – which are described in Ayurvedic texts. However the biological basis of prakriti had never been demonstrated though hypothesized (Bhushan, P., Kalpana, J. and Arvind, C., *J. Altern. Complement. Med.*, 2005, **11**(2), 349–353). In a recent multicentric study of 3416 subjects by institutions in Manipal, Hyderabad, Bengaluru and Pune, 262 individuals were selected for analysis using approximately one million genetic markers (SNPs) (Govindaraj, P. *et al.*, *Nature Commun.*, 2015, **5**, 15786). Following extensive genetic and statistical analysis, 52 genetic markers out of one million were identified, which were sufficient to differentiate the three prakritis – vata, pitta and kapha. Principal component analysis of the SNPs classified the 262 individuals into the vata, pitta and kapha groups, irrespective of their ancestry and backgrounds. A gene *PGMI* was also found to correlate with the phenotype of pitta. The findings suggested that prakriti has a genetic basis and the prakriti-based therapy is consistent with presonalized medicine. The genomic basis of prakriti received support from an epigenetic study based on DNA methylation for differentiating the three prakrits (Rotti, H. *et al.*, *J. Trans. Med.*, 2015, **13**, 151).

In a project on rasayana which is a division of Ayurveda consisting of procedures for promoting wellness and youthful ageing, the effect of amalaki rasayana (AR) was investigated. Swain *et al.* (*Mech. Ageing Dev.*, 2012, **133**(4), 112–117) showed that, compared to controls, the neurons and astrocytes in the brain of AR-fed rats had significantly less DNA damage, which affirmed the beneficial effect of AR on the maintenance of genomic stability. In a series of studies of AR on *Drosophila melanogaster*, Dwivedi *et al.* (*PLoS ONE*, 2012, **7**(5), e37113) demonstrated formulation-specific effects on several parameters of the fly's life, including size of the salivary gland, hnRNP levels in larval tissues, thermo tolerance of larvae/adult flies, median life span, starvation tolerance and fecundity. In another study, the authors showed that dietary supplement of AR suppressed neurodegeneration in fly models of Huntington's and Alzheimer's diseases without side effects (Dwivedi, V. *et al.*, *Curr. Sci.*, 2013, **105**(12), 1711–1723). They also showed that suppression of apoptosis by AR in the fly models of neurodegeneration applies only to induced apoptosis and not to developmental apoptosis (Dwivedi, V., Tiwary, S. and Lakhotia, S. C., *J. Biosci*., 2014, **40**(2), 1–17).

Panchakarma is a well-known procedure which attracts patients from India and abroad for the treatment of many disorders. Of the five procedures which constitute panchakarma, basti (enema) is most important and is used extensively in the treatment of obesity. In a joint study of 30 individuals with BMI above 30 kg/m^2 at Podar Hospital, ACTREC and Nair Hospital in Mumbai, it was reported that the subjects showed not only marked reduction in weight but also significant decrease in serum interferon (IFN)-Y and interleukin (IL6), and gradual reduction in IL8 level (Thatte, U. *et al.*, *Indian J. Med. Res.*, 2015, **142**(1), 53–62). They concluded that basti procedure reduces pro-inflammatory cytokines which are raised in obesity. The procedure modulates immune responses by regulating insulin resistance-causing pro-inflammatory cytokines, immunoglobulins and functional properties of T-cells.

To study the traditional methods of making Ayurvedic products and their effect on the composition and characteristics of the drug, Rasasindura made of mercury and sulphur was chosen by Ramanan *et al*. (*J. Synchrotron Radiat.*, 2015, **22**, 1233–1241) at BARC, Mumbai. Mercury-based drugs do not figure in ancient Ayurvedic texts and their use probably entered Ayurveda through Arab medicine in the 11th or 12th century. It was also used in Europe extensively despite known toxicity. However, it is no longer employed in therapeutics and is banned in many countries, even for use as dental amalgam. Nevertheless Ayurveda, and even more Siddha, has continued to use mercury-based drugs for centuries and claimed that drug toxicity is rare. To examine this riddle, a microstructural characterization of Rasasindura prepared by Arya Vaidya Sala, Kottakkal, according to the ancient protocol was done by X-ray absorption fine structure (XAFS). The study showed that Rasasindura has the same structure as non-toxic HgS and toxic chemical forms, viz. elemental Hg° and organo-Hg are completely absent in the study sample. Secondly, the nano-crystal ($D\text{-}_{Rasa} \approx 24$ mm) units of Rasasindura are robust, defect-free and also free of organic molecules. The absence of toxic chemical forms in the virgin medicine (before consumption) could account for its putative non-toxicity and its robust character would imply nanoparticle integrity during drug release. The authors concluded that 'Ayurvedic synthesis yielded a better controlled end product than laboratory-based red α-HgS with lower size dispersion and better ordered coordination configuration'.

The reported studies give us a flavour of research in Ayurvedic biology which is in its infancy. It is as rigorous as any branch of biology, but is distinct in so far as the inquiries are always based on cues from Ayurveda. This system of medicine prizes learning and the pursuit of knowledge, but urges that the reality of existence expresses itself not only in scientific insights and experiments but also in 'Man, the Unknown', who strides behind human endeavour as an unknown and unknowable determinant.

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